CLRN1 gene

clarin 1

Normal Function

The *CLRN1* gene provides information for making a protein called clarin 1. This protein is probably involved in normal hearing and vision. Clarin 1 has been found in several areas of the body, including sensory cells in the inner ear called hair cells. These cells help transmit sound and motion signals to the brain. This protein is also active in the retina, which is the light-sensing tissue that lines the back of the eye. Although the function of clarin 1 has not been determined, studies suggest that it plays a role in communication between nerve cells (neurons) in the inner ear and in the retina. Clarin 1 may be important for the development and function of synapses, which are junctions between neurons where cell-to-cell communication occurs.

Health Conditions Related to Genetic Changes

retinitis pigmentosa

Usher syndrome

At least 15 mutations in the *CLRN1* gene have been identified in people with Usher syndrome type III, which is characterized by a combination of hearing loss and vision loss. Some affected individuals also have problems with balance and coordination. *CLRN1* gene mutations cause a form of the condition known as Usher syndrome type IIIA (USH3A). This form of Usher syndrome is rare in most countries, although it represents about 40 percent of all Usher syndrome cases in the Finnish population.

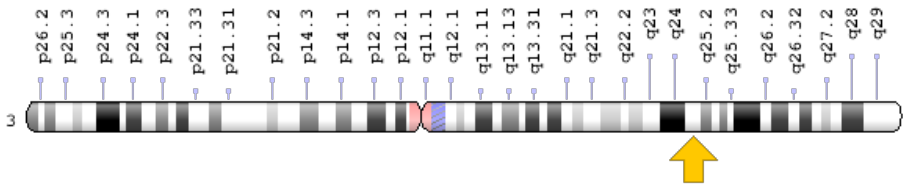
Several *CLRN1* gene mutations change single protein building blocks (amino acids) in the clarin 1 protein. In some cases, these mutations lead to the production of an abnormally short version of the protein or prevent the production of any functional clarin 1. Other mutations insert or delete small amounts of DNA in the *CLRN1* gene, which probably impairs the normal function of the protein. It is unclear how a missing or altered clarin 1 protein leads to the signs and symptoms of Usher syndrome type IIIA.

Two particular *CLRN1* gene mutations are most common in families of Finnish ancestry. One mutation, sometimes called Finmajor and written as Tyr176Ter or Y176X, leads to the production of an abnormally short, nonfunctional version of clarin 1. The other mutation, written as Met120Lys or M120K and also known as Finminor, substitutes the amino acid lysine for the amino acid methionine at protein position 120. This mutation appears to disrupt the protein's normal function.

Chromosomal Location

Cytogenetic Location: 3q25.1, which is the long (q) arm of chromosome 3 at position 25.1

Molecular Location: base pairs 150,926,163 to 150,972,999 on chromosome 3 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- USH3
- USH3A
- USH3A_HUMAN
- Usher syndrome 3A
- Usher syndrome type 3 protein

Additional Information & Resources

Educational Resources

- Neuroscience (second edition, 2001): Hair Cells and the Mechanoelectrical Transduction of Sound Waves
  https://www.ncbi.nlm.nih.gov/books/NBK10867/
- Neuroscience (second edition, 2001): The Retina
  https://www.ncbi.nlm.nih.gov/books/NBK10885/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28USH3A%5BTIAB%5D%29+OR+%28CLRN1%5BTIAB%5D%29%29+OR+%28%28USH3%5BTIAB%5D%29+OR+%28clarin+1%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- CLARIN 1
  http://omim.org/entry/606397

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=CLRN1%5Bgene%5D
- Hereditary Hearing Loss Homepage
  http://hereditaryhearingloss.org
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=12605
- Leiden Open Variation Database: CLRN1 Gene Mutations
  https://research.cchmc.org/LOVD2/home.php?select_db=CLRN1
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/7401
- RetNet: Summaries of Genes and Loci Causing Retinal Diseases: CLRN1
  https://sph.uth.edu/retnet/disease.htm#03.203d
- UniProt
  http://www.uniprot.org/uniprot/P58418

Sources for This Summary

- Adato A, Vreugde S, Joensuu T, Avidan N, Hamalainen R, Belenkiy O, Olender T, Bonne-Tamir B, Ben-Asher E, Espinos C, Millán JM, Lehesjoki AE, Flannery JG, Avraham KB, Pietrokovski S, Sankila EM, Beckmann JS, Lancet D. USH3A transcripts encode clarin-1, a four-transmembrane-domain protein with a possible role in sensory synapses. Eur J Hum Genet. 2002 Jun;10(6):339-50.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12080385
- Aller E, Jaijo T, Oltra S, Alió J, Galán F, Nájera C, Beneyto M, Millán JM. Mutation screening of USH3 gene (clarin-1) in Spanish patients with Usher syndrome: low prevalence and phenotypic variability. Clin Genet. 2004 Dec;66(6):525-9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15521980
- Fields RR, Zhou G, Huang D, Davis JR, Möller C, Jacobson SG, Kimberling WJ, Sumegi J. Usher syndrome type III: revised genomic structure of the USH3 gene and identification of novel mutations. Am J Hum Genet. 2002 Sep;71(3):607-17. Epub 2002 Jul 16.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12145752
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC449697/
- Geng R, Geller SF, Hayashi T, Ray CA, Reh TA, Bermingham-McDonogh O, Jones SM, Wright CG, Melki S, Imanishi Y, Palczewski K, Alagramam KN, Flannery JG. Usher syndrome IIIA gene clarin-1 is essential for hair cell function and associated neural activation. Hum Mol Genet. 2009 Aug 1; 18(15):2748-60. doi: 10.1093/hmg/ddp210. Epub 2009 May 3.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19414487
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2706682/

- Geng R, Melki S, Chen DH, Tian G, Furness DN, Oshima-Takago T, Neef J, Moser T, Askew C, Horwitz G, Holt JR, Imanishi Y, Alagramam KN. The mechanosensory structure of the hair cell requires clarin-1, a protein encoded by Usher syndrome III causative gene. J Neurosci. 2012 Jul 11; 32(28):9485-98. doi: 10.1523/JNEUROSCI.0311-12.2012.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22787034
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3422646/
- Isosomppi J, Västinsalo H, Geller SF, Heon E, Flannery JG, Sankila EM. Disease-causing mutations in the CLRN1 gene alter normal CLRN1 protein trafficking to the plasma membrane. Mol Vis. 2009 Sep 8;15:1806-18.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19753315
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2742642/
- Joensuu T, Hämäläinen R, Yuan B, Johnson C, Tegelberg S, Gasparini P, Zelante L, Pirvola U, Pakarinen L, Lehesjoki AE, de la Chapelle A, Sankila EM. Mutations in a novel gene with transmembrane domains underlie Usher syndrome type 3. Am J Hum Genet. 2001 Oct;69(4): 673-84. Epub 2001 Aug 27. Erratum in: Am J Hum Genet 2001 Nov;69(5):1160.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11524702
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1226054/
- Khan MI, Kersten FF, Azam M, Collin RW, Hussain A, Shah ST, Keunen JE, Kremer H, Cremers FP, Qamar R, den Hollander AI. CLRN1 mutations cause nonsyndromic retinitis pigmentosa. Ophthalmology. 2011 Jul;118(7):1444-8. doi: 10.1016/j.ophtha.2010.10.047. Epub 2011 Feb 18.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21310491

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/CLRN1

Reviewed: June 2016
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services